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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,649	06/04/2002	Pierre Belhumeur	1051-1-019	6750

7590 05/12/2009

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EXAMINER	
KIM, TAEYOON	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/980,649	BELHUMEUR ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 5-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 5-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/26/200 has been entered.

Applicant's amendment and response filed on 3/26/2009 has been received and entered into the case.

Claims 3 and 5-15 are pending and have been considered on the merits. All arguments have been fully considered.

Response to Amendment/Arguments

The declaration under 37 CFR 1.132 filed 3/26/2009 is insufficient to overcome the rejection of claims 3 and 5-15 based upon Safar et al. as set forth in the last Office action because:

The declaration by Dr. Michel Aigle states that the teaching of Safar et al. is focused on "conformation" of prion protein upon thermal treatment, and correlates loss of its infectivity, and Western blotting technology used by Safar et al. is not well adapted to this goal referring Fig. 1 of Safar et al., which apparently shows no significant change in quantity before and after treatment.

The current claims are drawn to a method of evaluating the efficiency of a

sterilization process using a yeast prion as an indicator, and determining the efficiency of the process by measuring the level of degradation of the indicator.

The argument is based on the finding that the technique of Safar et al. determining the "degradation" using Western blot technology does not show any degradation of the mammalian prion, especially based on Fig. 1 of Safar et al. It is correct that Western blot of Fig. 1 does not show any break-down or fragmentation (if this is what applicant interprets the term "degradation").

However, the claims of current application do not require whether Western blotting necessarily show any "degradation". The claims are drawn to an assay system measuring efficacy of a treatment, and in other words, some treatment would generate visible effect on the indicator when measured by a certain technology, while other treatment which might be not effective (such as thermal treatment of Safar et al.) to show such effect or the technology used for detecting would be not sensitive enough to show the difference. Nevertheless, the teaching of Safar et al. is interpreted that Western blotting can be used for bioassay for the determining the effect of thermal or any other treatment applied to the mammalian prion proteins. Therefore, whether or not Safar et al.'s Western blotting results show any degradation is not the limitation required by the current claims, and the bioassay of Safar et al. is certainly the way of evaluating the treatment to the mammalian prion proteins. It is well known in the art that protein break-down caused by certain treatment (thermal, enzymatic, etc.) can be detected by Western blotting technology or any other known technology (including CD spectrum as shown by Safar et al.) to show any structural change in proteins.

With regard to the "conformational change" of the mammalian prion as shown by Safar et al., applicant alleged that the conformational change is not degradation. The examiner pointed out in the previous office action that conformational change caused by thermal treatment is considered as "degradation" in broader interpretation. For example, denaturation is typically caused by heating or treating with chemical such as SDS, and the denaturation is considered as reduction in complexity, and therefore, the conformational change is interpreted as degradation.

Even if conformational change is not considered as degradation, it is reminded that the current claims do not require that the prion indicators to be degraded, rather the claims are drawn to determination whether there is any degradation, when various different sterilization techniques are employed.

Among various different sterilization techniques known in the art, some sterilization treatment would be effective to degrade or fragment the indicator, while others may not. Therefore, because Safar et al. do not show any degradation (i.e. fragmentation or decomposition) of mammalian prion protein by thermal treatment, it does not prevent the use of Western blotting technology to determine protein degradation upon different treatments are applied.

Applicant argued that Safar et al. do not measure degradation, rather it measures a conformational change. This argument is not persuasive because the use of Western blotting technology inherently provides information on proteins such as prion whether there is degradation (fragmentation or decomposition) upon various treatments. Simply because the results of Fig. 1 do not show any molecular weight shift or the intensity

change of the protein band, it does not mean that the Western blotting cannot detect degradation of prion proteins. This merely indicates that the thermal treatment is not effective for degrading (fragmenting or decomposing) prion proteins but it does not exclude the use of Western blotting technique for evaluating degradation of a protein. In fact, consisting with this view, the specification of the current application discloses that classical autoclave sterilization cycle was unable to destroy Sup35 protein (p.13-14), and thus Western blotting results showed no degradation (Fig. 4).

Applicant alleged that there are significant differences between yeast prion proteins and mammalian prion proteins, and there is still significant uncertainty regarding whether one of ordinary skill in the art could predict the utility of an invention based upon the teaching of Safar et al. using the proteins disclosed by Coustou et al., Glover et al. or Wickner et al.

This argument has been fully considered but found not persuasive. This argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See M.P.E.P. § 2129 and § 2144.03 for a discussion of admissions as prior art. Counsel's arguments cannot take the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964); and especially *In re Langer*, 183 USPQ 288 (CCPA 1974). See M.P.E.P. § 716.01(c) for examples of attorney statements that are not evidence and that must be supported by an appropriate affidavit or declaration.

Unless there is clear evidence showing that yeast prions are not considered as a counterpart of mammalian prions, the rejection is maintained. According to the review on prion by Prusiner (PNAS, 1998; of record), prions are extended to encompass yeast and other prions in which a similar mechanism of information transfer occurs (p.13378, left col.), and it is widely accepted that yeast prions behave the same way in terms of self-propagation, and thus yeast prions are widely used as a model for studying mammalian counterparts. Thus, a person of ordinary skill in the art would recognize that yeast prions can be considered as art-recognized equivalent to mammalian prions.

Applicant also argues that the effectiveness of ozone treatment, and ozone treatment goes beyond all the treatments described by Safar et al. as ozone is an extremely powerful oxidative process, able to break down chemical bonds. This argument is based on the features upon which applicant relies (i.e., superiority of ozone treatment in degrading prions) are not recited in the rejected claims in a way that this particular feature is required for the method. It is noted that ozone treatment is one of many different sterilization techniques known in the art, and the method of the current claims is drawn to evaluate any of such sterilization techniques, and does not require ozone treatment per se. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 5-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 discloses the limitation of "a sterilization process". It appears that the sterilization process is for prion proteins rather than sterilization of any molecule, microorganism, etc. Applicant is advised to amend the limitation to drawn to the sterilization process being effective to prion proteins. For example, claim 3 can be amended as "A method of evaluating the efficiency of a sterilization process on prion proteins comprising…"

Claim 7 discloses that the indicator is a biological indicator, a biochemical indicator or a chemical indicator. Claim 7 is dependent on claim 3, which discloses that the indicator is selected from SUP35, URE2 or HET-s. It is not clear whether these yeast prions are considered as biological, biochemical AND chemical indicator. The specification discloses that the biological indicators are usually composed of bacterial spores, and there is no disclosure such that yeast prions are biological indicators. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3 and 5-15 are rejected under 35 U.S.C. 103(a) as being unpatentable

over Safar et al. (1993) in view of Coustou et al. (PNAS, 1997), Glover et al. (Cell, 1997; IDS reference) or Wickner (Science, 1994).

Safar et al. teach a method of evaluating the effect of various treatments including thermal treatment and treatment with chemical scrapie inactivators such as formic acid, SDS, TFA, HFIP on scrapie prion protein (PrP27-30) film in a Petri dish (Table 1; Fig. 1; Materials and Methods) and Safar et al. use Western blotting analysis and CD spectrum (Fig. 1, 2, 4 and 5) for determining the effect.

Safar et al. do not teach the use of Sup35p, Ure2p or Het-s protein as an indicator.

Coustou et al. teach Het-s protein from *Podospora anserina* as an analog of a prion (see whole document).

Glover et al. teach Sup35p in *Saccharomyces cerevisiae* as a Yeast prion (see whole document). Glover et al. also teach an N-terminal fragment of Sup35p (residue 1-123) and a fragment NM comprising residues 1-253 (thus first 759bp of SUP35) of Sup35p (see Fig. 1), as well as a full-length Sup35p.

Wickner teaches the product of a chromosomal mutation in URE2 gene, called [URE3] is a prion form of Ure2p (see whole document).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use one of yeast prion analogs of Ure2p, Sup35p and Het-s protein taught by Wickner, Glover et al., and Coustou et al., respectively. This is because a person of ordinary skill in the art would recognize that the yeast prion

analogs have the same property as mammalian prion proteins, and thus suitable for replace the mammalian prion proteins as an indicator.

M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945) (Claims to a printing ink comprising a solvent having the vapor pressure characteristics of butyl carbitol so that the ink would not dry at room temperature but would dry quickly upon heating were held invalid over a reference teaching a printing ink made with a different solvent that was nonvolatile at room temperature but highly volatile when heated in view of an article which taught the desired boiling point and vapor pressure characteristics of a solvent for printing inks and a catalog teaching the boiling point and vapor pressure characteristics of butyl carbitol. "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.)".

Although Safar et al. in view of Wickner, Glover et al., or Coustou et al. do not particularly teach the amount of indicator being 0.1 ng to 100 g, the reference teaches the amount of scrapie prions in molarity. Safar et al. teach that the amount of prion protein (PrP27-30) used in the method is 0.9 nmol in total 150 µl of water, and the mean molecular weight of each residue is 109.5 (see page 2214; CD spectroscopy). Moreover, it is well known in the art and an inherent property of PrP27-30 to have about 142 amino acid residues supported by Prusiner (PNAS 1998, 95:13368-13383; see Fig. 2). Thus, a person of ordinary skill in the art can calculate the amount of PrP27-30 used

in the experiment, and it is about 140 μg (claim 11).

With regard to the new limitation of "in amyloid form" in claim 3, the yeast analogs of mammalian prion as taught by Wickner, Glover et al., or Coustou et al. are considered all amyloid form because it is well known in the art that only those gene products of yeast in amyloid or amyloid-like form are considered as prion counterparts, and therefore a person of ordinary skill in the art would use an amyloid form of yeast prion analogs in place for the mammalian prion of Safar et al.

With regard to various different sterilization techniques and assay systems determining the effect of the treatments listed in the current claims, the method of evaluating prion proteins after various treatment taught by Safar et al. is eventually determining the inactivation of prion proteins, a person of ordinary skill in the art would try other inactivation (sterilization) techniques known in the art to determine the effect on prion proteins. Furthermore, it would have been obvious to a person of ordinary skill in the art to try options well known in the art as assay techniques for protein analysis to determine the effect caused to the various sterilization techniques.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Safar et al. in view of Wickner, Glover et al., or Coustou et al. in further view of Feldman et al.

Claim 9 is directed to limitations to sterilization process of claim 3 being performed by sterilization techniques using low temperature gas plasma or oxidizing sterilizing agents.

Safar et al. in view of Wickner, Glover et al., or Coustou et al. teach the limitation of claim 3 (see above).

Safar et al. in view of Wickner, Glover et al., or Coustou et al. do not teach the use of low temperature gas plasma or oxidizing sterilizing agents for inactivation/sterilization process.

Feldman et al. teach the use of sterilization process to inactivate prion using oxidizing agents such as hydrogen peroxide as a form of low-temperature gas plasma (column 30, line 33 through column 34, line 42).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace the inactivation/sterilization process in the method of Safar et al. in view of Wickner, Glover et al., or Coustou et al. with a sterilization technique of Feldman et al. using oxidizing sterilizing agents.

The skilled artisan would have been motivated to make such a modification because conventional sterilization techniques taught by Safar et al. have disadvantage such that high temperature may cause damage and safety concerns and steam also can corrode metal materials. However, the sterilization technique of Feldman et al. is safer and has no detrimental effects on containers made of various materials.

The person of ordinary skill in the art would have had a reasonable expectation

of success in replacing sterilization technique of Safar et al. with that of Feldman et al. because such sterilization techniques of Feldman et al. is commercially available at the time of the invention made. For example, Sterrad system (Advanced Sterilization Products) using a sterilization technique of Feldman et al., which is commercially available.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 3, 9, 10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Safar et al. in view of Wickner, Glover et al., or Coustou et al. in further view of Dresdner Jr. et al.

Claims are directed to a limitation to sterilization process being performed by sterilization techniques using ozone-based exposure; a limitation to chemical exposure using sodium hydroxide; a limitation to a container being porous, permeable or semi-permeable.

Safar et al. in view of Wickner, Glover et al., or Coustou et al. teach the limitations of claim 3 (see above).

Safar et al. in view of Wickner, Glover et al., or Coustou et al. do not teach ozone-based exposure (claim 9), or sodium hydroxide as chemical exposure (claim 10).

Dresdner Jr. et al. teach the use of ozone (column 22, lines 44-52) or sodium hydroxide (column 27, line 48) as antiseptic composition.

It would therefore have been obvious for the person of ordinary skill in the art at

the time the invention was made to use antiseptic compositions of Dresdner Jr. in the method of Safar et al. in view of Wickner, Glover et al., or Coustou et al. to test the efficacy of these sterilization techniques in elimination of prion proteins.

A person of ordinary skill in the art would recognize the use of ozone or sodium hydroxide of Dresdner Jr. et al. as an art-recognized equivalent to the sterilization technique used by Safar et al. in view of Wickner, Glover et al., or Coustou et al.

M.P.E.P. §2144.06 states "In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a

photoconductor." 209 USPQ at 759.)."

Safar et al. in view of Wickner, Glover et al., or Coustou et al. do not teach the container being porous, permeable or semi-permeable.

Dresdner Jr. et al. also teach a porous and liquid-permeable medical glove for sterilization process (column 18, line 40; column 23, line 56).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace a glass container of Safar et al. with a medical glove of Dresdner Jr. et al.

The skilled artisan would have been motivated to make such a modification because contamination of prion proteins can happen in various different materials such as plastics, metal, or polymer, sterilization process should be carried out in various materials. Moreover, medical gloves are routinely used in hospitals and laboratories and are subject to prion contamination. Therefore, medical gloves of Dresdner Jr. et al. can be used in place of a glass container of Safar et al. to determine effectiveness of various prion sterilization techniques without damaging the material containing a prion protein.

The person of ordinary skill in the art would have had a reasonable expectation of success in replacing a glass container of Safar et al. with a medical glove of Dresdner Jr. et al. because medical gloves used in hospitals and laboratories are subject to routine sterilization to decontaminate pathogens such as prion.

Therefore, the invention as a whole would have been prima facie obvious to a

person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 4:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Taeyoon Kim
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